

**REMARKS**

Upon entry of the foregoing amendment, claims 65-90, 94-99, and 101-118 are pending for the Examiner's consideration, with claims 65, 80, 94, 103, 107, 108, 109, 114, 116, and 117 being the independent claims. Claims 65, 80, and 94 are amended herein. Claims 91-93 and 100 are cancelled herein. Claims 116 - 118 are sought to be added. Applicants respectfully submit that these amendments introduce no new matter. In this regard, the Examiner is referred to, for example, pages 4-5 and 20-22 of the application as originally filed.

***Rejections Under 35 U.S.C. § 103(a)******A. U.S. Patent No. 5,650,173***

The Examiner has rejected claims 65-115 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,650,173 ("the '173 patent"). Applicants respectfully submit that this rejection was improper as to claims 65-115 as previously presented, as well as to the claims as presented herein.

On page 3 of the Office Action, the Examiner states "Ramstack *et al.* [the '173 patent] do not specifically teach that the microparticles are 'maintained' at 'a certain temperature' for a 'certain period of time.' However, it is the position of the examiner that the cited reference still renders applicant's claimed process obvious." To provide the critical support needed for this rejection, the Examiner asserts on page 4 of the Office action that "it is within the ordinary skill of the pharmaceutical art to set aside a recently made batch of microparticles, allowing them to thoroughly dry, prior to using the microparticles in any further formulations. Additionally, it is within the knowledge of the ordinary artisan that increased dryness equals increased flowability." Applicants respectfully challenge the foregoing two assertions made by the Examiner under M.P.E.P. § 2144.03 C.

***(1) Challenge Under M.P.E.P. § 2144.03***

As explained in M.P.E.P. § 2144.03 by which the Examiner is bound, any facts noticed or asserted as within common knowledge should be "of notorious character and serve only to 'fill in the gaps' in an insubstantial manner which might exist in the evidentiary showing made by the examiner to support a particular ground for rejection." M.P.E.P. § 2144.03 E. The Examiner has provided no evidentiary showing with respect to the conditioning and maintaining steps of the claims of the present invention, because, as recognized by the Examiner, this subject

matter is lacking in the '173 patent. The assertions made by the Examiner regarding setting aside microparticles to thoroughly dry, and that increased dryness equals increased flowability, are not insubstantial assertions made to fill in the gaps. Rather, these assertions are the foundations upon which the rejection is based. It is never appropriate to rely solely on common knowledge in the art without evidentiary support in the record as the principal evidence upon which a rejection was based. *In re Zurko*, 258 F.3d 1379, 1386 (Fed. Cir. 2001); M.P.E.P. § 2144.03. Therefore, Applicants respectfully traverse under M.P.E.P. § 2144.03 C the following two assertions made by the Examiner, and, should the rejection be maintained, request that the Examiner provide documentary evidence in support of these assertions in the next Office Action.

(1) It is within the ordinary skill of the pharmaceutical art to set aside a recently made batch of microparticles, allowing them to thoroughly dry, prior to using the microparticles in any further formulations.

(2) It is within the knowledge of the ordinary artisan that increased dryness equals increased flowability.

**(2) *The Ramstack Declaration***

Applicants respectfully submit that the Examiner's assertion that "increased dryness equals increased flowability" is contradicted by the data presented in the above-captioned application. Filed herewith is a Declaration of J. Michael Ramstack, Ph.D. Under 37 C.F.R. § 1.132 ("the Ramstack Declaration"). As detailed in paragraph 3 of the Ramstack Declaration, the data presented for the Batch E microparticles (Table 3 on page 16 of the above-captioned application as originally filed) demonstrate that increased dryness can lead to decreased flowability. As detailed in paragraph 4 of the Ramstack Declaration, the data presented for the Batch F microparticles in Table 3 also demonstrate that increased dryness can lead to decreased flowability. Therefore, the Examiner's assertion that increased dryness equals increased flowability is refuted by the data presented in the above-captioned application itself.

The Examiner is taking the position that "set[ting] aside a recently made batch of microparticles, allowing them to thoroughly dry" is the same as the conditioning of the microparticles of the claimed invention. As noted in paragraph 4 of the Ramstack Declaration, such a position is refuted by the data presented in Table 3 for the Batch F microparticles. In particular, the Batch F microparticles demonstrate that conditioning the microparticles is not the same as drying microparticles since the conditioned microparticles had better flowability than the microparticles after being further dried under vacuum. Moreover, as explained in paragraph

5 of the Ramstack Declaration, microparticles made using the methods disclosed in the '173 patent may exhibit poor flowability, even though the microparticles were thoroughly dried, and that the process of the present invention was discovered as a way to improve the flowability of dry but poorly flowing microparticles.

Paragraph 6 of the Ramstack Declaration makes clear that even if microparticles are allowed to thoroughly dry, that alone is not a guarantee of good flowability. Paragraph 6 of the Ramstack Declaration also makes clear that increased dryness cannot be equated with increased flowability, and that conditioning the microparticles cannot be equated with drying the microparticles.

The Examiner asserts on page 4 of the Office Action that "there has been no criticality placed on the length of time the microparticles are maintained at this temperature, or on the flowability index, or the angle of repose." Applicants respectfully disagree with the Examiner, and assert that the above-captioned application is replete with discussions and data regarding the criticality of the angle of repose and the flowability index, and its relation to flowability. The Examiner is referred to, for example, pages 4, 5, 12-16, and 20-22 of the application as originally filed.

For at least the foregoing reasons, Applicants respectfully submit that this rejection under 35 U.S.C. § 103(a) could not properly be maintained as to claims 65-115 as previously presented, nor to the claims as presented herein.

Each of independent claims 65, 80, 94, 103, 107-109, and 116 as presented herein includes an affirmative step of measuring either the angle of repose or the flowability index. None of the documents cited by the Examiner discloses or suggests the measuring steps contained in the foregoing independent claims, or the more narrow claims depending therefrom. Independent claims 114 and 117 presented herein require that the microparticles have a specified angle of repose or flowability index, respectively, at the end of the maintaining step. None of the documents cited by the Examiner discloses or suggests a maintaining step resulting in microparticles having such an angle of repose or flowability index as recited in independent claims 114 and 117, or the more narrow claims depending therefrom. For at least this reason as well, Applicants respectfully submit that this rejection under 35 U.S.C. § 103(a) cannot properly be maintained for the claims as presented herein.

***B. The Conti Article***

The Examiner has also rejected claims 65-86, 88-111, and 113-115 under 35 U.S.C. § 103(a) as being unpatentable over “Use of polylactic acid for the preparation of microparticulate drug delivery systems” by Conti (“the Conti article”). The Examiner’s reasoning for the Conti article is substantially the same as described above for the ‘173 patent. The Examiner notes the same lack of teaching in the Conti article of the maintaining and conditioning steps of the present invention, and the Examiner makes the same unsupported assertions regarding setting aside microparticles to allow them to thoroughly dry, and that increased dryness equals increased flowability. As such, Applicants respectfully submit that the rejection based on the Conti article can not properly be maintained as to claims 65-115 as previously presented, nor to the claims as presented herein for at least all of the reasons detailed above. For brevity, Applicants respectfully incorporate by reference in this Section B for the Conti article all of the reasons detailed above in Section A for the ‘173 patent.

***Other Matters***

Applicants note that on page 2 of the Office Action under “Receipt of Papers” the Examiner states that the Preliminary Amendment and Supplemental Information Disclosure Statement were received on July 31, 2003. Applicants wish to clarify the record on the date of receipt of the Preliminary Amendment and Supplemental Information Disclosure Statement, and specifically request that the Examiner correct the records of the U.S. Patent and Trademark Office (PTO). Applicants filed the Preliminary Amendment and Supplemental Information Disclosure Statement on August 28, 2002, receipt of which by the PTO is evidenced by the attached copy of the date-stamped post card. Apparently, the papers filed by Applicants on August 28, 2002 were lost by the PTO, as an Office Action was issued by the Examiner on July 24, 2003 that did not reflect entry of the Preliminary Amendment filed August 28, 2002. Upon receipt of the Office Action mailed July 24, 2003, the undersigned contacted the Examiner to ascertain why the Preliminary Amendment had not yet been entered. The Examiner requested re-submission by the Applicants of the Preliminary Amendment and Supplemental Information Disclosure Statement, which was done on July 31, 2003, as evidenced by the attached copy of the date-stamped postcard re-submitting the documents. Applicants specifically request that the records of the PTO be corrected to reflect the original August 28, 2002 filing date for the Preliminary Amendment, and that the records make clear that the filing by Applicants of the

Preliminary Amendment did not result in the re-work of the office action by the Examiner. Rather, the re-work of the office action by the Examiner was necessitated by the PTO losing or otherwise not properly entering the Preliminary Amendment when it was filed on August 28, 2002.

The Examiner acknowledges receipt of the Supplemental Information Disclosure Statement originally filed on August 28, 2002, and indicates in the Office Action Summary that it is attached. However, Applicants have not received the initialed copy of the Form PTO/SB/08A filed on August 28, 2002. The Examiner is specifically requested to provide the initialed copy with the next written communication to the Applicants.

### *Conclusion*

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Dated: March 31, 2004

Respectfully submitted,

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